DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket N0. 77N–334S]

RIN 0905–AA06

Topical Drug Products for Over-the-Counter Human Use; Products for the Prevention of Swimmer's Ear and for the Drying of Water-Clogged Ears; Final Rule

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule establishing that any over-the-counter (OTC) topical otic drug product for the prevention of swimmer's ear or for the drying of water-clogged ears is not generally recognized as safe and effective and is misbranded. FDA is issuing this final rule after considering public comments on the agency's proposed regulation, which was issued in the form of a tentative final monograph, and all new data and information on OTC topical otic drug products for these uses that have come to the agency's attention. This final rule is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: August 15, 1995.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD–810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of December 16, 1977 (42 FR 63556), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC topical otic drug products, together with the recommendations of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in topical otic drug products. Interested persons were invited to submit comments by March 16, 1978. Reply comments in response to comments filed in the initial comment period could be submitted by April 14, 1978.

In accordance with § 330.10(a)(10), the data and information considered by the Panel, after deletion of a small amount of trade secret information, were placed on public display in the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

In the December 16, 1977 advance notice of proposed rulemaking on OTC topical otic drug products, the Panel discussed the treatment of swimmer's ear (42 FR 63556 at 63565), but the Panel did not address the prevention of swimmer's ear or the drying of water-clogged ears.

The agency's proposed regulation, in the form of a tentative final monograph, for OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears was published in the **Federal Register** of July 30, 1986 (51 FR 27366). Interested persons were invited to file by September 29, 1986, written comments, objections, or requests for oral hearing before the Commissioner of Food and Drugs regarding the proposal. Interested persons were invited to file comments on the agency's economic impact determination by November 28, 1986. New data could have been submitted until July 30, 1987, and comments on the new data until September 30, 1987.

In the **Federal Register** of November 7, 1990 (55 FR 46914), the agency published a final rule establishing that certain active ingredients that had been under consideration in a number of OTC drug rulemaking proceedings were not generally recognized as safe and effective. That final rule was effective on May 7, 1991, and included in § 310.545(a)(15) (21 CFR 310.545(a)(15)) the active ingredient acetic acid, which had been under consideration as part of this rulemaking for OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears. This ingredient was determined to be nonmonograph because no additional data had been submitted following publication of the tentative final monograph to determine whether acetic acid is generally recognized as safe and effective as a topical otic drug products for the prevention of swimmer's ear or for the drying of water-clogged ears. After that final rule published, only two ingredients remained to be evaluated in this rulemaking: Isopropyl alcohol and anhydrous glycerin. Final agency action on all other OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears occurs with the publication of this final rule.

In the tentative final monograph for OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears (51 FR 27366), the agency did not propose any active ingredient as generally recognized as safe and effective and not misbranded. However, the agency proposed monograph labeling in the event that data were submitted that resulted in the upgrading of any ingredient to monograph status. In this final rule, however, no active ingredient has been determined to be generally recognized as safe and effective for use in OTC topical otic drug products for the prevention of swimmer's ear or for the drying of water-clogged ears. Therefore, proposed §§ 344.3(c) through (f), 344.12, 344.14, 344.52, and 344.54 for OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears are not being issued as a final regulation.

This final rule declares OTC drug products containing active ingredients for the prevention of swimmer's ear or for the drying of water-clogged ears to be new drugs under section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)), for which an application or abbreviated application (hereinafter called application) approved under section 505 of the act (21 U.S.C. 355) and 21 CFR part 314 is required for marketing. In the absence of an approved application, products containing these drugs for this use also would be misbranded under section 502 of the act (21 U.S.C. 352). In appropriate circumstances, a citizen petition to establish a monograph may be submitted under § 10.30 (21 CFR 10.30) in lieu of an application.

This final rule amends part 310 (21 CFR part 310) to include OTC topical otic drug products containing active ingredients for the prevention of swimmer's ear or for the drying of water-clogged ears by adding new paragraph (a)(15)(ii) to § 310.545 to include the ingredients covered by this final rule, by redesignating the text of paragraph (a)(15) as (a)(15)(i), by revising the heading of newly redesignated paragraph (a)(15)(i), and by revising the heading of paragraph (a)(15) to clarify that products for the drying of water-clogged ears are also included. The inclusion of OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears in part 310 is consistent with FDA's established policy for regulations in which there are no monograph conditions. (See, e.g. §§ 310.510, 310.519, 310.525, 310.526, 310.532, 310.533, 310.534, and 310.536.) If, in the future, any ingredient is determined to be generally recognized as safe and effective for use in an OTC topical otic drug product for the

prevention of swimmer's ear or for the drying of water-clogged ears, the agency will promulgate an appropriate regulation at that time.

The OTC drug procedural regulations (21 CFR 330.10) now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph. Accordingly, FDA does not use the terms ''Category I'' (generally recognized as safe and effective and not misbranded), ''Category II'' (not generally recognized as safe and effective or misbranded), and ''Category III'' (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage. In place of Category I, the term ''monograph conditions'' is used; in place of Categories II or III, the term ''nonmonograph conditions'' is used.

In the tentative final monograph for OTC topical otic drug products (51 FR 27366 at 27367), the agency advised that the conditions under which the drug products are subject to the monograph would be generally recognized as safe and effective and not misbranded would be effective 12 months after the date of publication of the final monograph in the **Federal Register**. Although data and information were submitted in response to the proposed rule, they were not sufficient to support monograph conditions, and no monograph is being established at this time. Therefore, topical otic drug products that are subject to this rule are not generally recognized as safe and effective and are misbranded (nonmonograph conditions). Because no OTC drug monograph is being established for this class of drug products, the agency is adopting its standard 6-month effective date for the nonmonograph conditions in this final rule. Therefore, on or after August 15, 1995, no OTC drug products that are subject to this final rule may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved application.

In response to the proposed rule on OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears, two drug manufacturers submitted comments on isopropyl alcohol and anhydrous glycerin, and one physician submitted a comment on isopropyl alcohol and acetic acid. Copies of the comments received are on public display in the Dockets Management Branch (address above). Additional information that has come to the agency's attention since publication of the proposed rule is also on public display in the Dockets Management Branch.

I. The Agency's Conclusions on the Comments

A. General Comments

1. One comment contended that products for the treatment of ''water-clogged ears'' are not drugs within the meaning of section 201(g) of the act (21 U.S.C. 321(g)) and, thus, are not the proper subject of an OTC drug monograph. The comment stated that section 201(g)(1) of the act defines a drug, in part, as ''* * * (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals * * *.'' The comment argued that these products are not intended for use in connection with ''any disease,'' do not affect the structure or any function of the body, and are not meant to have any effect on the body. The comment mentioned that FDA had previously stated that ''water-clogged ears is not a recognized clinical entity or a term found in textbooks,'' (Refs. 1 and 2) and thus, in FDA's view, the condition ''water-clogged ears'' is not a disease.

The comment added that if FDA concluded that such products are intended for use in connection with a ''disease'' or affect the structure or a function of the body, then the products should be regulated as a device rather than as a drug. The comment stated that section 201(h) of the act (21 U.S.C 321(h)) states that a device ''does not achieve its primary intended purposes through chemical action within or on the body * * * and * * * is not dependent upon being metabolized for the achievement of its primary intended purposes.'' The comment contended that products that function by drying excess water work by a purely physical process and that the product is not metabolized.

Despite the comment's arguments, the agency considers products ''for the drying of water in the ears'' or ''to help relieve the discomfort of water-clogged ears by drying excess water'' to be drugs and not devices. All drugs do not need to be metabolized. Some work by a purely physical process, such as a skin protectant that forms a physical barrier.

The act defines a device, in section 201(h), in part, as an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is: (1) Recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The agency has determined that these products do not meet the definition of a device because they are not an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article.

As discussed in the Panel's report (42 FR 63556 at 63565), external otitis, an infection of the skin lining the external auditory canal, is one of the most common diseases of the ear. One type of external otitis is called ''diffuse external otitis'' and is commonly known as ''swimmer's ear.'' It occurs with greater frequency during hot, humid weather and has been reported to occur in divers and swimmers. ''Swimmer's ear'' is apparently due to excessive moisture in the external auditory meatus, which may be the result of various causes. The external auditory canal is a cul-de-sac, well suited for the collection of moisture, thus providing a basis for infection. Disruption of the skin lining of the external auditory canal by the action of the accumulated moisture, or by the use of instruments to clear the ear canal of water after bathing or swimming, may cause maceration, fissuring, or laceration of the skin lining and provide a favorable environment for the growth of bacteria or fungi. Although the action of products that dry water in the ear is limited to removal of the excess water, if this condition is left untreated, it could result in ''swimmer's ear.''

In the tentative final monograph (51 FR 27366 at 27367), the agency stated that it recognized a population that is prone to develop swimmer's ear and that the availability of OTC drug products to prevent the occurrence of this condition would benefit the consumer. Products that dry water in the ear may prevent the occurrence of ''swimmer's ear'' and, thus, help prevent disease. As discussed in the tentative final monograph (51 FR 27366 at 27370), the agency also believes that

excess water in the ear could impair hearing. Therefore, the drying of water-clogged ears may affect the function of the ear by reducing a loss of hearing in some individuals. Accordingly, the agency concludes that products that dry water in the ears are drugs under section 201(g) of the act.

References

(1) Letter from W. E. Gilbertson, FDA, to H. W. Gordon, Commerce Drug Co., Inc., coded LET006, Docket No. 77N–0334, Dockets Management Branch.

(2) Letter from W. E. Gilbertson, FDA, to H. W. Gordon, Commerce Drug Co., Inc., coded LET010, Docket No. 77N–0334, Dockets Management Branch.

2. One comment requested that products for drying water-clogged ears be allowed to make the claim ''helps relieve swimmer's ear.'' The comment stated that the agency's proposed definition of ''swimmer's ear'' in § 344.3(e) (51 FR 27366 at 27373) was too restrictive because it included a demonstration of effectiveness against external otitis in a susceptible target population. The comment mentioned that consumers have long used the term ''swimmer's ear'' to refer to the retention of excess water in the ears after swimming, showering, or bathing. The comment argued that a demonstration of efficacy against external otitis should not be a prerequisite for a claim relating to ''swimmer's ear.''

The agency disagrees with the comment. The Panel (42 FR 63556 at 63565) defined swimmer's ear as a ''diffuse external otitis,'' an infection of the skin lining the external auditory canal. Likewise, other medical experts (Ref. 1) define swimmer's ear as external otitis associate with swimming. Clinical symptoms include an itchy or painful, discharging ear, and a tender edematous canal filled with debris. *Pseudomonas aeruginosa* is the predominant bacterial pathogen in cases of external otitis. Successful treatment of the infection can require a combination of topical therapies, including antibiotics, steroids, drying agents, and acetic acid. If not successfully treated, swimmer's ear may lead to malignant external otitis and mastoiditis. For these reasons, the agency considers diagnosis and treatment of this infection by a physician to be necessary.

The comment did not submit any data to demonstrate that ear water-drying aid products alone ''help relieve swimmer's ear.'' Data showing effectiveness of an ear water-drying aid product as a single agent against external otitis would be a prerequisite for a claim relating to ''swimmer's ear.'' The agency concludes that the existing data are inadequate to support a relief of swimmer's ear claim for any ear water-drying aid drug product.

Reference

(1) Mandell, G. L., G. Douglas, and J. E. Bennett, ''Principles and Practice of Infectious Diseases,'' 3d ed., Churchill Livingstone, New York, pp. 1680–1681, 1990.

3. One comment requested that the proposed indications in § 344.52(b) for products for drying water-clogged ears be expanded to permit mention of the source of the water in the ears causing the problem. The comment suggested adding the following words to the indications: (''caused by'' or ''resulting from'') ''swimming, showering, or bathing.''

The agency would have no problems in allowing the indications to mention the source of the water. However, this would not be required information because the proposed indications adequately describe the use of the product. The agency would allow the source of the water to appear as optional additional information that could appear at the manufacturer's choice. At this time, indications for these products will not appear in the final rule because no active ingredients are included in a monograph for this class of OTC drug products. Should a monograph be proposed in the future, the optional expanded indications will be considered.

B. Comments on Isopropyl Alcohol and Anhydrous Glycerin

4. One comment submitted a study (Ref. 1) to support the effectiveness of 5 percent anhydrous glycerin in 95 percent isopropyl alcohol for the drying of water-clogged ears. The comment stated that if FDA determines that this product is a drug, it should be classified as Category I.

The agency has reviewed the study and determined that the data are insufficient to demonstrate the effectiveness of 5 percent anhydrous glycerin in 95 percent isopropyl alcohol for the drying of water-clogged ears. This study involved 27 male or female volunteers, between 18 and 65 years of age, with a history of water-clogged ears. The subjects were in generally good health with ears free of obstructions and tympanic membranes free of any perforations. The objective of the study was to determine the effectiveness of 5 percent anhydrous glycerin in 95 percent isopropyl alcohol placed in the external auditory canal to speed up the evaporation of water. Each subject was placed in the supine position, and the ear was inspected with an operating microscope. The ear to be tested was then filled with lukewarm water. Each subject was permitted to tilt his/her head to allow the water to run freely out of the ear onto absorbent cotton. Only those subjects with water remaining in their ears were selected. The presence of water was recorded on tape by means of an operating microscope and its television camera. Five drops of product or water, as a placebo, were then randomly instilled into the ear. The samples were coded to maintain a double-blind so that both the investigator and subjects were unaware of the material instilled. After 5 minutes, the ear was inspected under the operating microscope and the presence or absence of water was determined. The quantity of water present after treatment was recorded as ''more,'' ''same,'' ''less,'' or ''none.'' The findings were recorded on tape and the subject record form.

Because participants were selected based on a history of some problem with retaining water in the ears after exposure, it is the agency's view that it is inappropriate to use a water-only placebo in a study of the indication for relief of ''water-clogged ears.'' In such situations, the water-only group would be expected to do worse than a group left untreated after water exposure. The agency is also concerned that the method used in the study did not specify how the head was tilted nor did it specify the time allowed for the water to run freely out of the ear onto the absorbent cotton. The position of the head and the length of time allowed for the water removal from the ear should have been specified.

The agency does not consider a study population of 27 subjects adequate to demonstrate that the results are statistically significant. Based on its statistical evaluation of the results, the comment reported that the product was effective in 22 out of 25 subjects' ears (88 percent) and that the placebo was effective in 3 out of 24 subjects' ears (12 percent), a highly significant result (Chi Square $\leq$ 99.9 percent). However, the agency finds that a Yates correction of Chi Square should have been used for this small cell size study. A reanalysis using this correction was never provided.

While the study provides some supportive information on the product's drying effect, at least one additional well-designed confirmatory study with an adequate number of subjects is needed. Because the submitted data are inadequate to establish effectiveness for the drying of symptoms of water-clogged ears, neither anhydrous glycerin nor isopropyl alcohol is included in a monograph for this use. The agency's

detailed comments and evaluation of the above data are on file in the Dockets Management Branch (Ref. 2).

The agency considers this product to be a drug. (See discussion in section I.B., comment 5.) The agency has been informed that the comment plans to conduct another study to establish the effectiveness of this product for the drying of water-clogged ears (Refs. 3 and 4). When the study is completed, the comment should submit the data in the form of a petition to establish a monograph for this type of OTC drug product.

References

(1) Brookler, K. H., ''Evaluation of Auro-Dri in the Relief for Water-Clogged Ears,'' Comment No. C2, Docket No. 77N–334S, Dockets Management Branch.

(2) Letter from W. E. Gilbertson, FDA, to H. W. Gordon, Del Laboratories, coded LET5, Docket No. 77N–334S, Dockets Management Branch.

(3) Comment No. C5, Docket No. 77N–334S, Dockets Management Branch.

(4) Memorandum of meeting between representatives of Del Laboratories, Inc., and FDA, coded MM1, Docket No. 77N–334S.

5. One comment discussed the status of glycerin in a product containing 5 percent anhydrous glycerin in 95 percent isopropyl alcohol. The comment contended that glycerin was not an active ingredient, but that glycerin was the vehicle. The comment stated that the product did not make any claims for glycerin as an active ingredient and thus no further testing for the glycerin in this product was necessary. The comment stated that glycerin was miscible with both water and alcohol (Ref. 1) and, thus, glycerin was particularly appropriate for use as a vehicle in this product.

The comment pointed out that the agency had previously stated (Ref. 2):

> In order to meet the requirements for a combination product, each ingredient must be tested alone and also in combination to show effectiveness for the proposed claims. However, if glycerin functions only as a vehicle (and the need for it as a vehicle is shown) and no claims are made for it as an active ingredient, additional testing would not be required for this ingredient.

The comment added that the Panel stated in its report on OTC topical otic drug products (42 FR 63556 at 63562) that ''glycerin is used in topical otic products * * * as a vehicle because of its solvent properties. * * * Its viscosity makes it useful as an ingredient in both liquid and ointment forms of medication. * * * Glycerin is widely accepted as a vehicle of choice in otic products.''

The agency does not have sufficient information demonstrating that anhydrous glycerin functions only as a vehicle in this product. The anhydrous glycerin could have an active role in the product. One text states that anhydrous glycerin alone, or mixed with vinegar, will help to remove water from the ear (Ref. 3). The comment did not provide any data to show that at the 5 percent concentration present the anhydrous glycerin does not contribute to the effect of the product. In order to show that glycerin does not have an active role in the product, it needs to be shown that the product with the glycerin is not superior to 95 percent isopropyl alcohol used alone. If the combination is superior, this would show that the anhydrous glycerin contributes to the product's effectiveness. The agency believes that a four-arm study (combination, 95 percent isopropyl alcohol, anhydrous glycerin alone, and placebo, which would be no treatment) should be conducted to clarify the role of the glycerin in the product.

In addition, if the glycerin were found to act only as a vehicle, then the product would have to be labeled accordingly. The product could not continue to be labeled as 5 percent anhydrous glycerin in 95 percent isopropyl alcohol.

References

(1) ''The Pharmacological Basis of Therapeutics,'' 6th ed., edited by L. S. Goodman, and A. G. Gilman, The McMillan Co., New York, p. 951, 1980.

(2) Letter from W. E. Gilbertson, FDA, to H. W. Gordon, Commerce Drug Co., Inc., coded LET10, Docket No. 77N–0334, Dockets Management Branch.

(3) ''Handbook of Nonprescription Drugs,'' 10th ed., American Pharmaceutical Association, Washington, p. 400, 1993.

C. Comments on the Isopropyl Alcohol and Acetic Acid

6. One comment requested that a combination product containing 95 percent isopropyl alcohol and 3 percent acetic acid be included in the final monograph with a claim for the prevention of swimmer's ear. The comment urged the agency to consider this combination because isopropyl alcohol with anhydrous glycerin was proposed as category III for drying of water in the ears (51 FR 27366 at 27370) and 2 percent acetic acid in distilled water was category III for prevention of swimmer's ear (51 FR 27367). The comment stated that preliminary data from a study suggested that this product may be statistically significant in diminishing the frequency of otitis externa in children during the summer months. The comment concluded that a product containing 95 percent isopropyl alcohol and 3 percent acetic acid was effective in drying of excess moisture in the ears as well as re-establishing the acid mantle in the ear canals.

As the comment noted, in the tentative final monograph, the agency placed several products in category III: (1) 2 percent acetic acid in distilled water or propylene glycol and the combination of 5 percent anhydrous glycerin and 95 percent isopropyl alcohol for the prevention of swimmer's ear, and (2) the combination of 5 percent anhydrous glycerin and 95 percent isopropyl alcohol for the drying of water in the ears or for the relief of the discomfort of water-clogged ears by drying excess water.

The comment did not submit any data on this combination, nor was this combination considered by the Panel in its report or the agency in the tentative final monograph. More data were needed on all of these products. Likewise, adequate data to demonstrate the safety and effectiveness of the comment's product are needed. Because no data were submitted to establish safety and effectiveness, the combination of 95 percent isopropyl alcohol and 3 percent acetic acid for the prevention of swimmer's ear is not being included in a monograph.

II. The Agency's Final Conclusions on OTC Topical Otic Drug Products for the Prevention of Swimmer's Ear and for the Drying of Water-Clogged Ears

At this time, there is a lack of data from adequate and well-controlled studies to establish that acetic acid, isopropyl alcohol, anhydrous glycerin, or any other ingredients are safe and effective for use as a topical otic drug product for the prevention of swimmer's or for the drying of water-clogged ears.

Therefore, any ingredient that is labeled, represented, or promoted for OTC use as a topical otic drug product for the prevention of swimmer's ear or for the drying of water-clogged ears is considered nonmonograph and misbranded under section 502 of the act and is a new drug under section 201(p) of the act for which an approved application under section 505 of the act and part 314 of the regulations (21 CFR part 314) is required for marketing. In appropriate circumstances, a citizen petition to establish a monograph may be submitted under 21 CFR 10.30 in lieu of an application. Any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce after the effective date of this final rule that is not in compliance with the regulation is subject to regulatory action.

In the **Federal Register** of November 7, 1990 (55 FR 46914), the agency published a final rule in 21 CFR part

310, establishing that certain ingredients under consideration in a number of OTC drug rulemaking proceedings were not generally recognized as safe and effective. That final rule was effective on May 7, 1991, and included in § 310.545(a)(15) the ingredient acetic acid that had been previously considered under this rulemaking for use as a topical otic drug product for the prevention of swimmer's ear and for the drying of water-clogged ears. The agency is revising § 310.545(a)(15) to clarify that products for the drying of water-clogged ears are also included in the regulation and to add new paragraph (a)(15)(ii) to include the ingredients covered by this final rule.

III. Analysis of Impacts

No comments were received in response to the agency's request for specific comment on the economic impact of this rulemaking (51 FR 27366 at 27371). FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and, thus, is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. This particular rulemaking for OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears is not expected to pose such an impact on small businesses. As noted above, the ingredient acetic acid has already been removed from OTC topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears. The agency is only aware of several OTC topical otic drug products containing isopropyl alcohol and anhydrous glycerin labeled for these uses. Accordingly, based on the number of affected products, the agency certifies that this final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 310

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 310 is amended as follows:

PART 310—NEW DRUGS

1. The authority citation for 21 CFR part 310 continues to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 512–516, 520, 601(a), 701, 704, 705, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 360b–360f, 360j, 361(a), 371, 374, 375, 379e; secs. 215, 301, 302(a), 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 242(a), 262, 263b–263n).

2. Section 310.545 is amended by revising paragraphs (a)(15) and (d)(1) and by adding new paragraph (d)(18) to read as follows:

§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.

(a) * * *

(15) *Topical otic drug products for the prevention of swimmer's ear and for the drying of water-clogged ears*—(i) *Approved as of May 7, 1991.*

Acetic acid

(ii) *Approved as of August 15, 1995.*

Glycerin and anhydrous glycerin

Isopropyl alcohol

* * * * *

(d) * * *

(1) May 7, 1991, for products subject to paragraphs (a)(1) through (a)(2)(i), (a)(3) through (a)(4), (a)(6)(i)(A), (a)(6)(ii)(A), (a)(7) (except as covered by paragraph (d)(3) of this section), (a)(8)(i), (a)(9) through (a)(10)(iii), (a)(12)(i) through (a)(12)(iv), and (a)(14) through (a)(18)(i) of this section.

* * * * *

(18) August 15, 1995, for products subject to paragraph (a)(15)(ii) of this section.

* * * * *

Dated: January 31, 1995.

William K. Hubbard,

Interim Deputy Commissioner for Policy.

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